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Review

Burden of preventable cancers in India: Time to strike the cancer epidemic

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Abstract India has a rapidly growing population inflicted with cancer diagnosis. From an estimated incidence of 1.45 million cases in 2016, the cancer incidence is expected to reach 1.75 million cases in 2020. With the limitation of facilities for cancer treatment, the only effective way to tackle the rising and humongous cancer burden is focusing on preventable cancer cases. Approximately, 70% of the Indian cancers (40% tobacco related, 20% infection related and 10% others) are caused by potentially modifiable and preventable risk factors. We review these factors with special emphasis on the Indian scenario. The results may help in designing preventive strategies for a wider application.

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Background

Globally, cancer is increasingly being recognized as a major contributor to health concerns. The increasing age of populations, especially in the developing regions is an important factor, as cancer incidence increases directly with age. However, in India and similar countries, recent advancements in access to health care and therefore diagnosis are also important in documenting the role of cancer as a health problem. An estimated 13 million cancer cases are reported per year worldwide, and roughly 60% of these cases are expected to die in developing countries [1]. As per WHO projections, the death toll of cancer would reach 10 million cases per year worldwide by the year 2020. As per the recent estimates by India's National Cancer Registry Program (NCRP), 1.45 million cases would occur in 2016 with 0.74 million deaths in India. This is expected to rise to 1.73 million cases and 0.88 million deaths in 2020 [2]. Thus, one in 8 men and one in 9 women are expected to suffer from cancer [2] in their lifetime (considering a median life expectancy of 74 years).

Major potentially modifiable lifestyle factors include tobacco consumption in various forms, infections, dietary factors (which may be underestimated) and alcohol use. It is estimated that 35–50% of the cancer cases worldwide can be prevented by control of potentially modifiable factors [3,4]. While we acknowledge that variation in registry quality likely affects these results, we are struck by the observation that there is a wide geographic variation of cancer incidences among various cancer registries of India [2]. Aizwal (Capital of Mizoram state) records the highest cancer incidence in India of 270/100,000 population as compared to 40/100,000 population for Barshi (a rural area in Solapur district of Maharashtra state). Possibly, these wide variations implicate potentially controllable variations in lifestyle factors contributing to cancer risk. Such lifestyle variations might include variation in tobacco consumption, dietary factors and environmental factors that could be modified by targeted programs.

The etiological factors for preventable cancers may show wide country specific variations. Skin cancers (related to sun-exposure) are common in the western population but rare in Indians. Difference in patterns of tobacco consumption (smoked versus smokeless tobacco), alcohol consumption (spirits versus wines), and diet (less non-vegetarian and less consumption of red meat) leads to differences in incidence of related cancers too and mandates an India-centric approach to cancer prevention. In this article, we aim to discuss the burden of preventable cancer with special emphasis on the Indian scenario.

Tobacco

80% of the tobacco consumers reside in economically developing countries where there is little push to encourage prevention or help those who are already smokers. Many of them are of younger age group [3], especially men, but in India, where betel use is often combined with tobacco, it is important to acknowledge the contribution of smokeless tobacco in both men and woman. The incidence of tobacco related cancers varies widely as per geographic location and gender in India. 30–60% of total cancers among males and 10–30% among females are tobacco related by one estimate [2], so that 1 in 17 males and 1 in 50 females have a lifetime risk of tobacco related cancers in India [2]. This directly corroborates with a low proportion of tobacco consumption among females in India [5]. Alarming, 15% of the youth (age group 13–15 years) use tobacco in some form as per the Global Youth Tobacco Survey (GYTS 2009–10) [6]. Overall, 35% of adults (age ≥ 15 years; including 48% of males and 20% of females) use tobacco [5], typical as smoked tobacco (14% of adults; 25% of males and 3% of females) but 33% of males and 19% of females use smokeless tobacco (with or without smoking).

Tobacco increases the risk of lung cancer as well as 15 other cancers and is the forerunner of preventable causes of cancer deaths accounting for 21% of total cancer deaths worldwide [3]. It is the strongest risk factor for lung cancer (increasing risk by 10–20-fold for this extraordinarily lethal cancer) and also it has been implicated as a contributing etiological agent for head and neck cancers (oral cavity, nasal cavity, paranasal sinuses, nasopharynx, larynx, and hypopharynx), esophagus, stomach, colorectal, pancreatic, hepatocellular, bladder, kidney, cervical cancers and leukemia [7].

Yet another challenge in India is areca nut chewing along with betel leaves (locally known as pan) and which most times is stuffed with smokeless tobacco. Betel quid usage prevalence has been found to range from 20 to 40% in the Indian population [8]. Sweetened areca nut chewing habit has been found in school going children. Khandelwal et al. [9] in their study on 3896 children, found 27% chewing areca nut and mostly (80% of these) used sweetened form of it. Most of these children are unaware of the harmful effects of these habits.

Daily consumption of ten or more quids of pan-tobacco increases the risk of cancers of gingiva; the relative risk among males and females being 15.07 and 13.69, respectively [10]. Pan-tobacco habit of more than 40 years' duration also has a relative risk of 2.03 of developing carcinoma of esophagus [11].

It is important to note that tobacco cessation has many health benefits apart from prevention of cancer, such as in reducing cardiovascular and pulmonary diseases. Quitting smoking before 50 years of age reduces the risk of death by

50% as compared to those who continue smoking [12]. Tobacco cessation depends on a complex interplay of personal awareness, socio-cultural habits and governmental legislative actions. Strategies of tobacco control as advocated by WHO has been implemented by several countries including India. This includes a six-pronged strategy of **MPOWER** (Monitor tobacco use and prevention policy, Protect people from tobacco smoke, Offer help to quit tobacco, Warn about dangers of tobacco smoking, Enforce ban on tobacco advertising, promotion and sponsorship, Raise tax on tobacco). COTPA (Cigarette and other tobacco products Act 2003) states provisions for restriction of sale and use of tobacco products in India [13]. 18 Tobacco Cessation Centers (an initiative by WHO and supported by Govt. of India) are operational in various parts of country and is co-ordinated by National Institute of Mental Health and Neurosciences, Bangalore. The National Drug Dependence Center of All India Institute of Medical Sciences, New Delhi caters not only to the clinical care but also to community programs, education and research in this arena.

These programs depend on the enthusiasm and financial support of governmental agencies, but individual health care-takers, such as doctors, nurses and medical officers have much to contribute, having the direct interaction with the subject. Simply mnemonic may be helpful to keep in mind. At an individual level, for those who seek to quit, 5 “A” method should be used (Ask, Advise, Assess, Assist and Arrange) and for those not yet willing to quit, 5 “R” method should be used (Relevance of quitting, Risk of continuing tobacco, Rewards of quitting, Roadblocks to quitting and Repeat these at each visit). Depending on the level of addiction and motivation of the users to quit, behavioral counseling or pharmacotherapy or a combination of both may be required. Lastly, the efforts and practices for tobacco cessation should also apply to betel quid chewing (which as discussed is also of a major concern in the Indian population).

Alcohol

As per an estimate by WHO [14], 30% of total population in India consumed alcohol (compared to a global figure of 38.3%). The per capita consumption has increased from 1.6 liters in 2003–2005 to 2.2 liters in 2010–2012. As compared to global figures of 16%, heavy/binge drinking was noted in 11% of population.

Alcohol contributes to around 4% of all cancers worldwide. Alcohol consumption leads to increased risk of squamous cell carcinoma of mouth, pharynx, larynx, and esophagus in multiple studies and the reports have been fairly consistent. Risk for some other cancers like adenocarcinoma of esophagus, gastro-esophageal junction, gastric cardia, colon, rectum and pancreas has also been found to be increased with alcohol [15].

A prospective study [16] found an increased risk by 6% per consumption of 10 g/day of alcohol. Its use increased the risk of oropharynx, larynx, esophagus, rectum, liver and breast cancers (study restricted to women). The EPIC study (The European Prospective Investigation into Cancer and Nutrition) found 10% attributable cancer risk associated with alcohol in men and 3% in women [17]. In this study, high alcohol consumption was set at 2 or more drinks per day (24 g of alcohol) in men and 1 or more drink per day (12 g of alcohol) for women.

Studies pertaining to association of alcohol with cancer in the Indian population are limited. Sankaranarayanan et al. found significantly ($p < 0.001$ for all these studies) increased risk of gingival cancers [18], esophageal cancers [11] and laryngeal cancers [19] with alcohol consumption in their case-control studies; relative risk being 2.62, 2.33 and 2.58 respectively for gingival, esophageal and laryngeal cancers.

Laws enforced by the government for limiting alcohol use includes heavy excise tax on sale of alcohol, fixing the legal age for consumption and prohibition of alcohol use in certain states of country. However, the law varies from state to state. The pattern of alcohol consumption in India has shown a transition over the last 3–4 decades. While, alcohol drinking and abuse was limited to poor socio-economic class, now alcohol is being propagated as a mark of the affluent society. Peer pressure and social cultures are making the dynamics of alcohol consumption complex. Most of the efforts by government and non-government organizations focus on tobacco; awareness and educational programs pertaining to harmful effects and restriction of alcohol should be propagated. Putting constraints on hours of sale, days of sale, sale around premises of school, colleges and institutions may also be helpful as initial constraint measures. Putting specific warning labels (similar to that on cigarettes) on alcoholic packaging, restricting advertisement and sponsorship and regulating prices of alcoholic drinks as compared to local beverages could be a further stepping stone toward a better alcohol control policy.

Infections

Infection related cancers (example: stomach, cervix, hepatocellular) accounts for around 20–25% of all the cancer cases worldwide, but the burden is especially high in the developing world where infection-prevention practices are limited, wherein 80% of these cases reside [1].

Most common infections associated with cancer are viruses and include Human Papilloma virus (HPV), Hepatitis B & C, Human T-cell lymphotropic virus (HTLV-1), Human Immunodeficiency virus (HIV), Human herpes virus 8 and Epstein-Barr virus. However, non-viral infections are important, prominently including *Helicobacter pylori* and some helminthes (*Opisthorchis viverrini*, *Clonorchis sinensis* and *Schistosoma haematobium*).

Data from the Indian population addressing specifically at infections related cancers are sparse. HPV related cancer incidences in India are provided by ICO (Institut Català d'Oncologia) Information center on HPV [20]. As per the report, the proportion of cancers considered HPV related in India varies from 20% (cervical cancers) to <1% for anal and vaginal/vulva cancers. HPV related head and neck cancers are reported to be 5% among males and 1.1% among females. The importance of cervical cancer deserves special mention. In cervical cancers, 80–85% have HPV 16/18 detected, emphasizing its importance in the etiology of this cancer. While early recognition often leads to cure, too few women are identified as at risk.

India has 34 million carriers of Hepatitis B, an extraordinary frequency which accounts for 10–15% of world's carrier population [21]. Considering the risk of hepatocellular carcinoma in carriers of hepatitis B and C (approximately 1–3% over 30 years), the future burden of these cancers will likely

be enormous. Hepatocellular cancer is difficult to detect early and very likely to be fatal.

Approximately, 2.4 million Indians are said to be living with HIV, likely an underestimate. Non-Hodgkin lymphoma are most common among HIV associated malignancy and risk of cervical, anal, vulva/vaginal and penile cancer risk appear to be increased based on limited data from the Indian population [22]. The incidence of Kaposi sarcoma seems to be low in the Indian population [23].

The prevalence of *Helicobacter pylori* infection has been found to be high (50–80%) in the Indian population not corroborating with the incidence of gastric cancers and this is known as “Indian Enigma” [24]. This could partly be because of the mildly pathogenic variants of bacteria (NAB47 and NAD1) in the Indian population and also because of other factors (like dietary, tobacco and socio-economic status) which may overwhelm and at times mask the effect of this oncogenic infection [24].

Majority of infections causing cancers are transmitted sexually (HPV, hepatitis and HIV). Practicing safe sex would help to prevent majority of these infections. Sexual education as a part of elementary education and inculcating concepts of safe sexual practices among individuals through IEC (information education and communication) systems should be promoted. Promotion of use of condoms are already advertised as means to reduce HIV infections; addition of information that this would also prevent potential risk of development of cancer would increase awareness as well as may increase their use in population at large. These oncogenic infections are also spread by infected blood or body fluids, wherein minimal exposures have a high transmission risk. Unsanitary office, clinic and hospital practices will contribute to this transmission. Following universal guidelines for screening and transfusion of blood and blood products, and especially, using disposable needles and syringes will greatly help reduce exposure. Effective vaccination strategies also exist for Hepatitis and HPV infections but are expensive in areas of limited resources. Use of highly active anti-retro viral therapy (HART), interferon and nucleoside/tide analogs decreases viral loads in HIV and hepatitis and impact on the transmission of these onco-viruses in the population (as well as having major treatment benefits, including reduction in cancer risk).

Physical inactivity, diet and obesity

At least 6 cancers (colorectal, breast, stomach, liver, kidney and endometrial) have direct links with unhealthy diets, physical inactivity and obesity [25], although we acknowledge that the evidence is only association, not causal. Where interventions would change cancer risk is unclear, because poor diet/inactivity is associated with many other lifestyles that increase cancer risk (e.g., smoking). Prospective intervention studies are difficult to conduct in the population.

Physical inactivity

5% of cancer deaths are attributable to physical inactivity. Evidence supporting reduction of risk with an increase in physical activity is the strongest with breast, colo-rectal cancers and endometrial cancers while there are still some data to suggest a

benefit for gastrointestinal cancers, prostate and endometrial cancers.

Dallal et al. [26] reported association between recreational physical activity and risk of invasive/in-situ breast cancer in California Teachers Study. Women with strenuous activity (>5 vs. ≤ 0.5 h/week/year) had statistically significant reduction of both invasive (RR 0.80; 95% CI 0.69–0.94; $p = 0.02$) as well as in-situ breast cancer risk (RR 0.69; 95% CI 0.48–0.98; $p = 0.04$). Overweight women in this study also showed lower risks of breast cancer death irrespective of estrogen receptor status and disease stage (RR 0.53; 95% CI, 0.35–0.80) [19]. A meta-analysis of 52 studies [27] showed an inverse association between physical activity and colon cancer (RR of 0.76; 95% CI: 0.72, 0.81). Voskuil et al. [28] in a systemic review of studies which included 7 cohort and 13 case-control studies found a majority (80%) of 10 high quality studies showed a risk reduction of $>20\%$.

Ambivalent findings

Daily total physical activity was associated with fewer incidences of carcinoma stomach, colon, liver and pancreas in a Japanese public health center prospective study [29]. Antonelli et al. [30] in a prospective cohort of 190 men undergoing prostatic biopsy found a lower likelihood of positive biopsy result in men performing at least 9 or more metabolic equivalent task (MET) hours/week (OR 0.35, CI 0.17–0.75, $p = 0.007$) and they were also less likely to have higher grade of disease (Gleason 7 or greater, OR 0.14, CI 0.02–0.94, $p = 0.04$).

In contrast, Patel et al. [31] evaluated men from the American Cancer Society Cancer Prevention Study II Nutrition Cohort and based on 5503 prostate cancers reported in 72,174 men found no association between recreational physical activity and prostate cancer risk. However, >35 MET/week was associated with less aggressive prostate cancers as compared to those with no activity (RR, 0.69; 95% confidence interval, 0.52–0.92; P for trend = 0.06). There is also some suggestion that this benefit could be limited to particular racial groups like whites as compared to blacks. Singh et al. [32] reported in their prospective study on 307 men that the whites with ≥ 9 MET/week were less likely to receive a positive biopsy result as compared to those with <9 MET/week (OR 0.47; 95% CI, 0.22–0.99; $P = 0.047$), however the same was not true for the black population.

Studies on the Indian population are limited in this aspect. Mathew et al. [33] evaluated the role of household activities (HA) in the development of breast cancer. Odds ratio for ≥ 6 h/day spent on HA as compared to 3 h/day was 0.70 for premenopausal and 0.51 for postmenopausal women. As per the study, it is estimated that proportion of breast cancers avoided in urban and rural women with moderate or high HA could be as high as 19% and 38% respectively.

Diet

A variety of food has been studied in relation to cancer. Dietary fat (some association with prostate cancer), dairy products (ovarian cancer), soy (decreased risk of breast cancer with 20 mg per day of isoflavone), fruits (decreased risk of prostate cancer with lycopene), vegetables and fibers have all shown weak association and controversial results in various studies and have not been shown to affect cancer risk [34]. Vitamins

and micro-nutrients have a controversial role in relation to cancer causation and prevention [35]. Vitamin D (serum levels > 25 nmol/L) and Calcium intake (1200 mg/day) may confer doubtful protection against colon cancers. Beta-carotene (increases risk of lung cancers), Vitamin E (increase risk of prostate cancer), selenium (decreased risk of overall cancer) have all failed to establish a clear association with cancer etiology or prevention.

Although the mechanism of carcinogenicity of red (pork, beef, and lamb) and processed meat (sausages, hot dogs, bacon and salami) is not clear, studies have shown an association with increased risk of colo-rectal cancers. The International Agency for Research in Cancer (IARC) working group [36] reported an increased risk by 17% per 100 g/day of red meat and 18% per 50 g/day of processed meat for colon cancer and identified these as potential carcinogens. Red meat (HR 1.22, 95% CI 1.16–1.29) and processed meat (HR 1.12, 95% CI 1.06–1.19) were also associated with elevated risk for cancer mortality [37]. This might be of more concern in the western population as compared to the Indian population (consumption of red and processed meat is < 20%).

Indian diet and cancer

The Indian diet is unique owing to its diversity, cultural and religious practices. Turmeric (Curcumin) and other spices and food additives (cumin, chillies, Kalakhar, Amrita Bindu, etc.) have been found to have cancer preventive properties [38]. Curcumin (a component of the Indian spice Turmeric), cumin seeds and basil leaves have been found in animal studies to have significant suppressive effect on cancer induction by dietary benzopyrene [39,40]. Amrita Bindu (a salt-spice-herbal mixture) has been found to protect rats against cancer induced by N-methyl-N-nitrosoguanidine [41]. Vegetarian diet (primarily composed of cereals and pulses) forming the major diet of Indians have been found to be associated with low cancer risk as compared to a non-vegetarian diet [42,43].

Deep fried cooking at high temperature (which generates polycyclic aromatic hydrocarbons), dried fish (consumed in parts of South India and Eastern part of India), and spicy food have been implicated in causation of stomach cancer in the Indian population [44,45]. Carcinoma esophagus has been found to be in high prevalence in the north eastern part of

the country and studies have shown this to be associated with consumption of betel quid chewing, sun dried vegetables, chillies and spicy food [46,47]. Rajkumar et al. [48] noted a high risk of oral cavity cancers in subjects who consumed meat, ham or salami (processed and fried meat) two or more times a week.

Obesity

36% American adults and 17% of American children are obese [49]. Although, obesity has not been a concern in the Indian population until recently, the scenario is changing. As per the National Family Health Survey [50], 12% of males and 16% of females in India are either obese or overweight and this may further increase in future. It has also been reported that body mass index (BMI) may not be a true representative of burden of obesity and ill effects of obesity might be evident even at a lower BMI (≥ 25 kg/m²) in the Indian population and this may be an increasing concern [51].

Obesity (BMI of ≥ 30 kg/m²) has been associated with increased risk of several cancers including non-Hodgkin's lymphoma, leukemia, multiple myeloma, and cancers of the kidney, colon, rectum, breast (in postmenopausal women), pancreas, ovary, and prostate [52]. It accounts for approximately 8% (10% in men and 6% in women) of all cancers. A meta-analysis of prospective observational studies [53] suggested strong association of esophageal adenocarcinoma, thyroid cancer and renal cancers in men and endometrial and gall bladders cancers additionally in women with an increase in BMI of 5 kg/m². Based on a large population based cohort study of 5.2 million UK adults, it is estimated that around 41% of all endometrial cancers and 10% or more of gallbladder, kidney, liver, and colon cancers were associated with excess weight [54]. An increase in population wide BMI by 1 kg/m² could lead to an increase in annual cancer cases by 4000 patients [54], if this association is truly etiological.

Singh et al. in a hospital based matched case-control study on the Indian population found that overweight (BMI 25–29.9) and obese (BMI ≥ 30) have an odds ratio of 1.06 and 2.27 respectively as compared to normal weight women in developing breast cancer [55].

Screening and preventive strategies: India centric approaches

The modifiable risk factors may have different priorities in the western and Indian population (Table 1) and region-specific approaches may be needed. The diversity in socio-economic strata, health care policy prioritization and public health delivery system in India may pose difficult challenges in implementing the screening and preventive strategies established in the western world. In this section, we discuss strategies tailored to the Indian population based on evidence.

Results of screening and preventive trials in India

Carcinoma of breast, uterine cervix and lip and oral cavity together constitutes around 34% of all cancers in India [56]. Although limited studies are available, the results nevertheless are promising in some regard.

In a cluster randomized trial, Sankaranarayanan et al. reported a reduction in cancer incidence by 25% and cervical

Table 1 Compares and contrasts the modifiable risk factors for causation of cancer in the western and Indian population.

Developed world (western population)	Developing Country (Indian population)
<ul style="list-style-type: none"> • Tobacco smoking (cigarettes and cigars) • Alcohol (spirits, wine) • Red and processed meat • Obesity (body mass index ≥ 30 kg/m²) • Human immunodeficiency virus, Hepatitis virus, Human Papilloma virus associated head and neck cancers (in that order) • Sun exposure associated skin cancers 	<ul style="list-style-type: none"> • Smokeless tobacco in various forms; smoked tobacco • Alcohol (local made, spirits) • Deep fried, salted fish, spicy food • Obesity (body mass index ≥ 25 kg/m²) • Human Papilloma virus associated cervical cancer, Human immunodeficiency virus, Hepatitis virus (in that order) • Uncommon in Indian population

cancer mortality by 35% after single round of screening with visual inspection with acetic acid by a trained health care personnel [57]. Another large scale study showed a reduction in cervical cancer mortality with a rate ratio of 0.69 ($p = 0.003$) after 12 years of follow up and four rounds of screening with acetic acid and visual inspection [58]. Sankaranarayanan et al. showed a 53% reduction in advanced cervical cancer diagnosis and 48% reduction in deaths compared to standard group in women (30–59 years) screened with single round of HPV testing [59].

Oral cancer screening with visual inspection by a trained health worker (three rounds at three year intervals) showed a reduction in oral cancer incidence of 38% and 81% reduction in mortality (in those who complied to all the three rounds) as compared to the control group [60].

Sankaranarayanan et al. recently reported on the impact and immunogenicity of HPV vaccination in girls in India [61]. Unmarried girls aged 10–18 years were recruited in this study and were planned to receive 3 doses of quadrivalent HPV vaccine on days 1, 60 and 180 or 2 doses on day 1 and 60. However, because of a variety of reasons, many girls received 1 or 2 doses of vaccine alone. Immune response of 2 doses were found to be non-inferior to 3 doses and also did not show any difference in the incident cases of cervical carcinoma in these groups.

Cost effectiveness of preventive strategies in India

Although, cost effectiveness analysis pertaining to India alone is not available, Goldie et al. used computer based models to assess the cost effectiveness of cervical cancer screening strategy in five developing countries including India. The authors estimated screening women once in their lifetime at the age of 35 years (with a one-visit or two visit screening involving visual inspection of cervix with acetic acid or DNA testing for HPV in cervical cell samples) may lead to a reduction in lifetime risk by 25–36% and would cost less than 500 United States Dollars (USD) per year of life saved [62]. Oral cancer screening by visual inspection by a trained health care worker would cost less than six USD per persons (over approximately 10 years) and could lead to incremental (i.e. the difference between intervention and control arms) cost per life year saved of 835 USD for all individuals and 156 USD for high risk individuals [63].

An analysis by Okonkwo et al. showed that estimated cost-effectiveness ratio for a single clinical breast examination (CBE) in women of age group 40–60 could be 793 US Dollars per life year gained and 1341 US Dollars per life year gained if CBE was done biennially in the same age group [64].

Resource stratified strategies for the Indian scenario

Based on the results of the studies done on the Indian population and the cost-effectiveness of the techniques, we could recommend strategies suited to needs and resources of our country [65]. Conventional Pap smear and HPV testing considered the standard screening method for carcinoma cervix may not be applicable to the Indian scenario. A practical approach could be screening with visual inspection and acetic acid in women aged 30–49 years and HPV testing in those more than 30 years of age (as permitted by the available resources).

Efforts should be made to screen women at least once in their lifetime after 30 years of age.

Oral cancer screening with visual inspection by a trained auxiliary health care worker could be a cost-effective screening policy. Individuals at high risk (those consuming tobacco products, alcohol or betel nut) in a specific age group (30–60 years) could be given most priority. These individuals (because of their tobacco and alcohol behavior) are also at increased risk for non-communicable diseases (NCDs) and hence, this screening opportunity can be used to screen them for common NCDs like hypertension and diabetes mellitus.

Based on the studies on the Indian population, in lieu of the mammographic screening, clinical breast examination every 5 years or biennially is predicted to reduce breast cancer mortality rates by 8% and 16% respectively and this could also be done in an inexpensive manner [64]. CBE with diagnostic ultrasonography could be an approach in women younger than 50 years of age. If resources permit use of screening with mammography, women aged 50–65 years should be given preference.

As supported by the study on Indian girls [61], 2 doses of quadrivalent HPV vaccination (6 months apart) could be a realistic and sustainable approach toward widespread application.

Government initiative for preventable cancers in India: integrative approach

NCDs accounts for 60% of all the death worldwide. In India, it accounts for around 50% of all deaths and cancer accounts for 1/5th of all NCDs [66]. Keeping in view the common risk factors for NCDs, Government of India (GOI) has merged the National Cancer Control Program into NPCDCS (National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke) with an aim to prevent and control common NCDs through behavior and lifestyle changes, to provide early diagnosis and management of common NCDs, to build capacity at various levels of health care facilities for prevention, diagnosis and treatment of common NCDs, to develop trained human resource within Public Health set up and to establish and develop capacity for palliative & rehabilitative care. 100 districts are expected to be strengthened for early detection and management of cancers and over 1000 health personnel in various categories of manpower would be trained. This would also provide baseline data about cancer incidence at district and state levels which would further help in designing effective strategies effectively focused on preventable causes of cancers in India.

Conclusion

A multipronged strategy is needed to tackle the growing burden of cancer in India and striking the preventable cancer burden could be the best long term approach. Preventable cancers could comprise up to 60–70% of the total cancer burden in India. Concerns specific to the Indian population are smokeless tobacco, areca nut chewing (often with tobacco), country made liquors and infections (mostly ano-genital HPV and Hepatitis). Unique dietary habits (deep fried and spicy food) coupled with increasing burden of obesity and a propensity of the population toward physical inactivity is also a growing

area of concern. Lack of nationwide screening guidelines and vaccination strategies are further hurdles in inciting an attack on these preventable cancers.

Tobacco control law and program needs to be prioritized and implemented effectively across all states of the country. Apart from government initiatives, advocacy by civil society and efforts of non-government organizations also needs to be promoted in this regard. Cost-effective strategies for screening could include screening of women (30–49 years of age) with visual inspection and acetic acid; oral cancer screening with visual inspection by a trained health care worker in high risk individuals; and clinical breast examination biennially in specific age groups (40–60 years). Although, this strategy is not evidence based, this could be an inexpensive, practical and resource stratified approach. Similarly, one or two doses of quadrivalent HPV vaccine in girls (9–26 years) could be a widely applicable vaccination strategy.

In summary, the unique challenges of preventable cancer burden in India may be dealt with indigenous and India-specific approaches which may result in a sustainable long term control of cancer.

Conflicts of interests

None.

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References

- [1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011;61:69–90.
- [2] Three year report of population based and hospital based cancer registries (2012–2014). Released online ahead of print. <<http://www.ncdirindia.org/>> [accessed 22.05.2016].
- [3] Brawley OW. Avoidable cancer deaths globally. *CA Cancer J Clin* 2011;61:67–8.
- [4] Colditz GA, Wolin KY, Gehlert S. Applying what we know to accelerate cancer prevention. *Sci Transl Med* 2012;28(4):127rv4.
- [5] Global adult tobacco survey fact sheet 2009–2010. Available on <http://www.searo.who.int/tobacco/data/india_rtc_reports/en/> [accessed 22.05.2016].
- [6] Global youth tobacco survey fact sheet 2009–10. Available on <http://www.searo.who.int/tobacco/data/india_rtc_reports/en/> [accessed 22.05.2016].
- [7] Sasco AJ, Secretan MB, Straif K. Tobacco smoking and cancer: a brief review of recent epidemiological evidence. *Lung Cancer* 2004;45(Suppl 2):S3–9.
- [8] Gupta PC, Ray CS. Epidemiology of betel quid usage. *Ann Acad Med Singapore* 2004;33:31–6.
- [9] Khandelwal A, Khandelwal V, Saha MK, Khandelwal S, Prasad S, Saha SG. Prevalence of areca nut chewing in the middle school-going children of Indore, India. *Contemp Clin Dent* 2012;3:155–7.
- [10] Sankaranarayanan R, Duffy SW, Padmakumary G, Day NE, Padmanabhan TK. Tobacco chewing, alcohol and nasal snuff in cancer of the gingiva in Kerala, India. *Br J Cancer* 1989;60:638–43.
- [11] Sankaranarayanan R, Duffy SW, Padmakumary G, Nair SM, Day NE, Padmanabhan TK. Risk factors for cancer of the oesophagus in Kerala, India. *Int J Cancer* 1991;49(4):485–9.
- [12] Murthy P, Saddichha S. Tobacco cessation services in India: recent developments and the need for expansion. *Indian J Cancer* 2010;47(Suppl 1):69–74.
- [13] <<http://www.tobaccocontrolaws.org/legislation/country/india/summary>> [accessed 22.05.2016].
- [14] <http://www.who.int/substance_abuse/publications/global_alcohol_report/profiles/en/#I> [accessed 22.05.2016].
- [15] Thomas DB. *Environ Health Perspect* 1995;103(Suppl 8):153–60.
- [16] Allen NE, Beral V, Casabonne D, Kan SW, Reeves GK, Brown A, et al. Moderate alcohol intake and cancer incidence in women. *J Natl Cancer Inst* 2009;101(5):296–305.
- [17] Schütze M, Boeing H, Pischon T, Rehm J, Kehoe T, Gmel G, et al. Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. *BMJ* 2011;7(342):d1584.
- [18] Sankaranarayanan R, Duffy SW, Padmakumary G, Day NE, Padmanabhan TK. Tobacco chewing, alcohol and nasal snuff in cancer of the gingiva in Kerala, India. *Br J Cancer* 1989;60(4):638–43.
- [19] Sankaranarayanan R, Duffy SW, Nair MK, Padmakumary G, Day NE. Tobacco and alcohol as risk factors in cancer of the larynx in Kerala, India. *Int J Cancer* 1990;45(5):879–82.
- [20] <<http://www.hpvcentre.net/summaryreport.php>> [accessed 22.05.2016].
- [21] Biggar RJ, Chaturvedi AK, Bhatia K, Mbulaiteye SM. Cancer risk in persons with HIV/AIDS in India: a review and future directions for research. *Infect Agent Cancer* 2009;4:4.
- [22] Puri P. Tackling the hepatitis B disease burden in India. *J Clin Exp Hepatol* 2014;4(4):312–9.
- [23] Kumarasamy N, Vallabhaneni S, Flanagan TP, Mayer KH, Solomon S. Clinical profile of HIV in India. *Indian J Med Res* 2005;121(4):377–94.
- [24] Misra V, Pandey R, Misra SP, Dwivedi M. Helicobacter pylori and gastric cancer: Indian enigma. *World J Gastroenterol* 2014;20(6):1503–9.
- [25] Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med* 2003;348:1625–38.
- [26] Dallal CM, Sullivan-Halley J, Ross RK, Wang Y, Horn-Ross PL, Deapen D, et al. Long-term recreational physical activity and risk of invasive and in situ breast cancer: the California teachers study. *Arch Intern Med* 2007;167(4):408–15.
- [27] West-Wright CN, Henderson KD, Sullivan-Halley J, Ursin G, Deapen D, Neuhausen S, et al. Long-term and recent recreational physical activity and survival after breast cancer: the California teachers study. *Cancer Epidemiol Biomarkers Prev* 2009;18(11):2851–9.
- [28] Voskuil DW, Monninkhof EM, Elias SG, Elias SG, Vlems FA, Leeuwen FE van. Task force physical activity and cancer. Physical activity and endometrial cancer risk, a systematic review of current evidence. *Cancer Epidemiol Biomarkers Prev* 2007;16(4):639–48.
- [29] Inoue M, Yamamoto S, Kurahashi N, Iwasaki M, Sasazuki S, Tsugane S. Japan public health center-based prospective study group. Daily total physical activity level and total cancer risk in men and women: results from a large-scale population-based cohort study in Japan. *Am J Epidemiol* 2008;168(4):391–403.
- [30] Antonelli JA, Jones LW, Bañez LL, Thomas JA, Anderson K, Taylor LA, et al. Exercise and prostate cancer risk in a cohort of veterans undergoing prostate needle biopsy. *J Urol* 2009;182(5):2226–31.
- [31] Patel AV, Rodriguez C, Jacobs EJ, Solomon L, Thun MJ, Calle EE. Recreational physical activity and risk of prostate cancer in a large cohort of U.S. men. *Cancer Epidemiol Biomarkers Prev* 2005;14(1):275–9.

- [32] Singh AA, Jones LW, Antonelli JA, Gerber L, Calloway EE, Shuler KH, et al. Association between exercise and primary incidence of prostate cancer: does race matter? *Cancer* 2013;119(7):1338–43.
- [33] Mathew A, Gajalakshmi V, Rajan B, Kanimozhi VC, Brennan P, Binukumar BP, et al. Physical activity levels among urban and rural women in south India and the risk of breast cancer: a case-control study. *Eur J Cancer Prev* 2009 Sep;18(5):368–76.
- [34] Key TJ. Fruits and vegetables and cancer risk. *Br J Cancer* 2011;104(104):6–11.
- [35] Vastag B. Nutrients for prevention: negative trials send researchers back to drawing board. *J Natl Cancer Inst* 2009;101(7):446–51.
- [36] Bouvard V, Loomis D, Guyton KZ, Grosse Y, Ghissassi FE, Benbrahim Tallaa L, et al. International agency for research on cancer monograph working group. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol* 2015;16(16):1599–600.
- [37] Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. Meat intake and mortality: a prospective study of over half a million people. *Arch Intern Med* 2009;169(6):562–71.
- [38] Sinha R, Anderson DE, McDonald SS, Greenwald P. Cancer risk and diet in India. *J Postgrad Med* 2003;49(3):222–8.
- [39] Aggarwal BB, Kumar A, Bharti AC. Anticancer potential of curcumin: preclinical and clinical studies. *Anticancer Res* 2003;23:363–98.
- [40] Aruna K, Sivaramakrishnan VM. Anticarcinogenic effects of some Indian plant products. *Food Chem Toxicol* 1992;30:953–6.
- [41] Shanmugasundaram KR, Ramanujam S, Shanmugasundaram ER, Amrita Bindu-a salt-spice-herbal health food supplement for the prevention of nitrosamine induced depletion of antioxidants. *J Ethnopharmacol* 1994;42:83–93.
- [42] Rajaram S, Sabate J. Health benefits of a vegetarian diet. *Nutrition* 2000;16:531–3.
- [43] Rao DN, Ganesh B, Rao RS, Desai PB. Risk assessment of tobacco, alcohol and diet in oral cancer-a case-control study. *Int J Cancer* 1994;58:469–73.
- [44] Mathew A, Gangadharan P, Varghese C, Nair MK. Diet and stomach cancer: a case-control study in South India. *Eur J Cancer Prev* 2000;9:89–97.
- [45] Rao DN, Ganesh B, Dinshaw KA, Mohandas KM. A case-control study of stomach cancer in Mumbai, India. *Int J Cancer* 2002;99:727–31.
- [46] Phukan RK, Chetia CK, Ali MS, Mahanta J. Role of dietary habits in the development of esophageal cancer in Assam, the north-eastern region of India. *Nutr Cancer* 2001;39:204–9.
- [47] Nayar D, Kapil U, Joshi YK, Sundaram KR, Srivastava SP, Shukla NK, et al. Nutritional risk factors in esophageal cancer. *J Assoc Physicians India* 2000;48:781–7.
- [48] Rajkumar T, Sridhar H, Balaram P, Gajalakshmi V, Vaccarella S, Nandakumar A, et al. Oral cancer in Southern India: the influence of body size, diet, infections and sexual practices. *Eur J Cancer Prev* 2003;12(2):135–43.
- [49] <https://en.wikipedia.org/wiki/Obesity_in_the_United_States> [accessed 22.05.2016].
- [50] <<http://dhsprogram.com/publications/publication-frind3-dhs-final-reports.cfm>> [accessed 22.05.2016].
- [51] Shetty PS. Nutrition transition in India. *Public Health Nutr* 2002;5(1A):175–82.
- [52] Pan SY, Johnson KC, Ugnat AM, Wen SW, Mao Y. Canadian cancer registries. Epidemiology research group. Association of obesity and cancer risk in Canada. *Am J Epidemiol* 2004;159(3):259–68.
- [53] Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet* 2008;371(9612):569–78.
- [54] Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5 24 million UK adults. *Lancet* 2014;384(9945):755–65.
- [55] Singh P, Kapil U, Shukla N, Deo S, Dwivedi S. Association of overweight and obesity with breast cancer in India. *Indian J Community Med* 2011;36(4):259–62.
- [56] Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0. Cancer incidence and mortality worldwide: IARC cancerbase. No.11. Lyon, France: International Agency for Research on Cancer; 2012. <<http://globocan.iarc.fr>> 2013 [accessed 26.05.2016].
- [57] Sankaranarayanan R, Esmy PO, Rajkumar R, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *Lancet* 2007;370:398–406.
- [58] Mitta I, Mishra GA, Singh S, et al. A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. *Int J Cancer* 2010;126:976–84.
- [59] Sankaranarayanan R, Nene BM, Dinshaw KA, et al. Osmanabad District Cervical Screening Study Group. A cluster randomized controlled trial of visual, cytology and human papillomavirus screening for cancer of the cervix in rural India. *Int J Cancer* 2005;116:617–23.
- [60] Sankaranarayanan R, Ramadas K, Thara S, et al. Long term effect of visual screening on oral cancer incidence and mortality in a randomized trial in Kerala. *India Oral Oncol* 2013;49:314–21.
- [61] Sankaranarayanan R, Prabhu PR, Pawlita M, Gheit T, Bhatla N, Muwonge R, et al. Immunogenicity and HPV infection after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre prospective cohort study. *Lancet Oncol* 2016;17:67–77.
- [62] Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin MahéC, Wright TC. Alliance for cervical cancer prevention cost working group. Cost-effectiveness of cervical-cancer screening in five developing countries. *N Engl J Med* 2005;353(20):2158–68.
- [63] Subramanian S, Sankaranarayanan R, Bapat B, Somanathan T, Thomas G, Mathew B, Vinoda J, Ramadas K. Cost-effectiveness of oral cancer screening: results from a cluster randomized controlled trial in India. *Bull World Health Organ* 2009;87(3):200–6.
- [64] Okonkwo QL, Draisma G, der Kinderen A, Brown ML, de Koning HJ. Breast cancer screening policies in developing countries: a cost-effectiveness analysis for India. *J Natl Cancer Inst* 2008;100(18):1290–300.
- [65] Rajaraman P, Anderson BO, Basu P, Belinson JL, Cruz AD, Dhillon PK, et al. Recommendations for screening and early detection of common cancers in India. *Lancet Oncol* 2015;16(7):e352–61.
- [66] <<http://mohfw.nic.in/index1.php?lang=1&level=3&sublinkid=3627&lid=2194>> [accessed 22.05.2016].